TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED / ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	US APPLICATION NO (if known, see 37 CFR 1.5)
P67280US0	09/926496

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/GB00/01807	11 May 2000	13 May 1999

TITLE OF INVENTION

NICOTINE DELIVERY SYSTEMS

APPLICANT(S) FOR DO/EO/US

David Leslie MCNEIGHT

Applicant herein submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for Internatl. Preliminary Examination was made by the 19th month from earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the Internatl. Preliminary Examination report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:
    International Search Report EPO
    PCT/IB/304 Form
    PCT/IB/308 Form
    First Page of Publication
    International Preliminary Examination Report - with no annexes

US APPLICATION NO.(If known, see 37 CFR 1 5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/926496	PCT/GB00/01807	P67280US0

	CALCULATIONS	PTO USE ONLY
17. ☒ The following fees are submitted:		
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Internatl. prelim. examination fee paid to USPTO (37 CFR 1.492 (a) (1)) . . $710.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (2)) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) . . $740.00		
Neither international preliminary examination fee (37 CFR 1.492 (a) (3)) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO) **$1040.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (4)) and all claims satisfied provisions of PCT Article 33(2)-(4) $100.00		
Search Report prepared by the EPO or JPO (37 CFR 1.492 (a) (5)) **$890.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of $130.00 for furnishing the **oath or declaration** later than ☐ **20** ☒ **30** months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 130.00	

Claims	**Number Filed**	**Number Extra**	Rate		
Total Claims	**16** - 20 =	-0-	x $18.00	$	
Independent Claims	1 - 3 =	-0-	x $84.00	$	
Multiple Dependent Claim(s) (if applicable)			+ $280.00	$	
TOTAL OF ABOVE CALCULATIONS =				$ 1020.00	
Reduction by 1/2 for filing by **small entity**, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$ 1020.00	
Processing fee of $130 for furnishing the **English translation** later than ☐ **20** ☐ **30** months from the earliest claimed priority date (37 CFR 1.492(f))				$	
TOTAL NATIONAL FEE =				$ 1020.00	
Fee of $40.00 for recording the enclosed **assignment** (37 CFR 1.21(h)). Assignment must be accompanied by appropriate cover sheet (37 CFR 3.28, 3.31).				$	
TOTAL FEES ENCLOSED =				$ 1020.00	
				Amt. to be refunded:	$
				Amt. charged:	$

a. ☒ A check in the amount of $ 1020.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. **06-1358** in the amount of $ ____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge my account any additional fees set forth in §1.492 during the pendency of this application, or credit any overpayment to Deposit Account No. **06-1358**. A duplicate copy of this sheet is enclosed.

SEND ALL CORRESPONDENCE TO:

JACOBSON HOLMAN PLLC
400 7th Street, N.W., Suite 600
Washington, DC 20004
202-638-6666
CUSTOMER NUMBER: 00136

By Jonathan L. Scherer
Jonathan L. Scherer
Reg. No. 29,851

JPH&S 3/95

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: David Leslie MCNEIGHT

Serial No.: New

Filing Date: November 13, 2001

For: NICOTINE DELIVERY SYSTEMS

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

IN THE SPECIFICATION

On page 1, immediately following the title, please insert the following sentence: --This is a nationalization of PCT/GB00/01807 filed May 11, 2000 and published in English.--

Please incorporate the new Abstract of the Disclosure into the specification, submitted herewith on a separate sheet.

IN THE CLAIMS

Please amend claims 3, 5, 9, 12, 14 and 16 as follows:

3. (amended) A nicotine delivery system according to claim 1, in which the microcapsules comprise yeast cells.

5. (amended) A nicotine delivery system according to claim 1, presented in a solid carrier from the surface of which

microcapsules are gradually released for controlled delivery.

9. (amended) A system according to claim 7, having such a size, solubility and charge of nicotine that it delivers, in use over a time period between 4 and 20 minutes, an amount of nicotine equivalent to that delivered by a cigarette.

12. (amended) A system according to claim 1, comprising a flavouring substance.

14. (amended) A system according to claim 1, comprising a vitamin supplement.

16. (amended) A system according to claim 1, comprised in a patch.

REMARKS

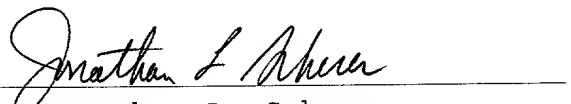
The foregoing Preliminary Amendment is requested in order to delete the multiple dependent claims and avoid paying the multiple dependent claims fee and to place the application in better form for examination.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Early action on the merits is respectfully requested.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By 
Jonathan L. Scherer
Reg. No. 29,851

400 Seventh Street, N.W.
Washington, D.C. 20004-2201
(202) 638-6666

Atty. Docket: P67280US0
Date: November 13, 2001
JLS/cmf

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

3. (amended) A nicotine delivery system according to claim 1 [or claim 2], in which the microcapsules comprise yeast cells.

5. (amended) A nicotine delivery system according to claim 1 [any one of claims 1 to 4], presented in a solid carrier from the surface of which microcapsules are gradually released for controlled delivery.

9. (amended) A system according to claim 7 [or claim 8], having such a size, solubility and charge of nicotine that it delivers, in use over a time period between 4 and 20 minutes, an amount of nicotine equivalent to that delivered by a cigarette.

12. (amended) A system according to claim 1 [any one of claims 1 to 11], comprising a flavouring substance.

14. (amended) A system according to claim 1 [any one of claims 1 to 13], comprising a vitamin supplement.

16. (amended) A system according to claim 1 [any one of claims 1 to 4], comprised in a patch.

Abstract

There is disclosed a delivery system for nicotine comprising nicotine encapsulated in a microcapsule system which releases the encapsulated nicotine on contact of the microcapsules with a nicotine solvent.

NICOTINE DELIVERY SYSTEMS

This invention relates to delivery systems for nicotine.

Nicotine is commonly taken in the form of smoking tobacco, in cigarettes, principally, cigars and pipe tobacco. To a lesser extent, tobacco, or a preparation from it, is chewed. More rarely, nowadays, is snuff taken. Smoking is declared to be injurious to health, though nicotine itself, in appropriate quantity, is not harmful in the way smoking is, which is due to components other than the nicotine in cigarette smoke and may even be beneficial - it is reported on numerous occasions as aiding concentration.

Though some question it, nicotine is generally regarded as addictive - certainly, increasing taxes on tobacco, Government health warnings and high profile lawsuits brought against tobacco companies by those made terminally ill, or their bereaved, seem to do little to reduce consumption.

There are several products commercially available to help those wishing to quit smoking. These take the form of tablets, chewing gum and patches, all of which are intended to deliver nicotine without the generation of smoke and its associated carcinogenic or otherwise harmful components.

A problem with formulating such products is that nicotine itself is a quite volatile liquid with a boiling point as low as 123° - 125°C at atmospheric pressure, and this makes it difficult to incorporate in products on account of evaporation losses during formulation and the need to seal the products against evaporation of the nicotine for a reasonable shelf life. At the same time, the nicotine must be readily released on use - in the mouth, in the case of gum or lozenge, or through the skin in the case of a patch.

The manner of injection of nicotine is by dissolving in fatty tissue. Nicotine is not readily absorbed in the gut, and no product is intended to be swallowed.

Patches are, of course, somewhat clinical, and while no doubt quite effective, not aesthetically pleasing. Gum is widely regarded as anti-social, often as much so as smoking - there is a disposal problem involved with gum which by and large its users ignore, which has led to its being outlawed in Singapore, a measure which other countries may well follow. Of all the approaches, the most aesthetically acceptable - lozenges, which leave nothing to dispose of and which can be sucked without the sometimes highly objectionable masticating movements - are perhaps the most difficult to formulate, requiring usually elevated temperature processing, leading to nicotine loss through evaporation and an uncertain final dose in the lozenge, and special protection against evaporation from the finished product, if a reasonable shelf life is to be had.

The present invention provides a nicotine delivery system that avoids problems of the prior art and which can give rise to improved products across the available range, but particularly in regard to the lozenge.

The invention comprises a delivery system for nicotine comprising nicotine encapsulated in a microcapsule system which releases the encapsulated nicotine on contact of the microcapsules with a nicotine solvent.

The nicotine solvent that may be targeted could be the fatty tissue of the buccal cavity.

The microcapsules may comprise yeast cells. The system may comprise a mixture of cells charged with nicotine and diluent, empty cells.

The system may be presented in a solid carrier from the surface of which microcapsules are gradually released for controlled delivery.

The solid carrier may comprise a saliva-soluble or dispersible substance, and may comprise a lozenge, which may be sugar-based. The lozenge may have such a size, solubility and charge of nicotine that it delivers a dosage of nicotine, in use over a time period between 4 and 20 minutes, equivalent to that delivered by a cigarette. The lozenge may be elongate, between 5 and 20 cm in length and snappable as by having preferential snapping positions into a number of portions each capable of comfortable accommodation in the mouth.

The solid carrier may, however, comprise a chewing gum.

The system may comprise a flavouring substance, which may also be encapsulated in a microcapsule system, and may also comprise a vitamin supplement, which also may be encapsulated in a microcapsule system.

The system may be comprised in a patch.

Nicotine delivery systems according to the invention and embodiments of products including the same will now be described with reference to the accompanying drawings, in which:-

Figure 1 is a diagrammatic illustration of a method of preparing microencapsulated nicotine;

Figure 2 is a view of one embodiment of a lozenge product; and

Figure 3 is a view of a second embodiment of a lozenge product.

Figure 1 of the drawings illustrate a method for preparing a delivery system for nicotine comprising nicotine encapsulated in a microcapsule system which releases the encapsulated nicotine on contact of the microcapsules with a nicotine solvent.

Nicotine, in the form of liquid nicotine acid 11, is poured into a mixing vessel 12 with a paddle 13. A measured amount of nicotine is mixed into a given volume of yeast cells 14 in order to give a reasonably concentrated absorption of nicotine into each yeast cell. A suitable mix is 25 g nicotine, 50 g of yeast cells, and 100 g of water. This is stirred for 1-24 hours at about 40°C. Cells are removed by centrifugation and dried. An expected loading is between 25 and 60% by weight of nicotine into the cells, depending on the mix used.

The thus nicotine loaded yeast cells 14 are then poured from the vessel 12, in a second stage of the process, into a larger volume of yeast cells 14 in a second mixing vessel 15, also with a paddle 13, and the mixture stirred.

Thus will a desired concentration of nicotine encapsulated in yeast cells be obtained.

The mixed loaded and diluent yeast cells 14 are then incorporated into products with appropriate quantities of the yeast to give the desired nicotine dose in the product.

Two such products are illustrated in Figures 2 and 3.

Figure 2 illustrates an ingot-shaped candy bar 21 which might be some 9 or 10 cm long so as to fit into a packet such as cigarettes are sold in. The bar 21 has transverse grooves 22 enabling it to be snapped into bite-size pieces.

Figure 3 illustrates a similar product 31, this time shaped more like a cigarette, again with grooves 32 for snapping. The presentations of Figures 2 and 3 were first suggested in GB 2 299 756 A.

These products, which are quite similar to cigarettes and which may be used either as aids to quitting smoking or as cigarette substitutes where smoking is not permitted, will, by virtue of their loaded yeast content, contain an equivalent nicotine does to that delivered by smoking a cigarette.

Flavourings such for example as mint, Scotch whisky, Cognac or menthol can also be added, again encapsulated in similar fashion to the yeast, as can other beneficial agents such as vitamin supplements.

CLAIMS

1. A delivery system for nicotine comprising nicotine encapsulated in a microcapsule system which releases the encapsulated nicotine on contact of the microcapsules with a nicotine solvent.

2. A nicotine delivery system according to claim 1, in which the nicotine solvent comprises fatty tissue of the buccal cavity.

3. A nicotine delivery system according to claim 1 or claim 2, in which the microcapsules comprise yeast cells.

4. A nicotine delivery system according to claim 3, comprising a mixture of cells charged with nicotine and diluent, empty cells.

5. A nicotine delivery system according to any one of claims 1 to 4, presented in a solid carrier from the surface of which microcapsules are gradually released for controlled delivery.

6. A system according to claim 5, in which the solid carrier comprises a saliva-soluble or dispersible substance.

7. A system according to claim 6, in which the solid carrier comprises a lozenge.

8. A system according to claim 7, in which the lozenge is sugar-based.

9. A system according to claim 7 or claim 8, having such a size, solubility and charge of nicotine that it delivers, in use over a time period between 4 and 20 minutes, an amount of nicotine equivalent to that delivered by a cigarette.

10. A system according to claim 9, in which the lozenge is elongate, between 5 and 20 cm in length and snappable as by having preferential snapping positions into a number of portions each capable of comfortable accommodation in the mouth.

11. A system according to claim 5, in which the solid carrier comprises a chewing gum.

12. A system according to any one of claims 1 to 11, comprising a flavouring substance.

13. A system according to claim 23, in which the flavouring substance is also encapsulated in a microcapsule system.

14. A system according to any one of claims 1 to 13, comprising a vitamin supplement.

15. A system according to claim 14, in which the vitamin is also encapsulated in a microcapsule system.

16. A system according to any one of claims 1 to 4, comprised in a patch.

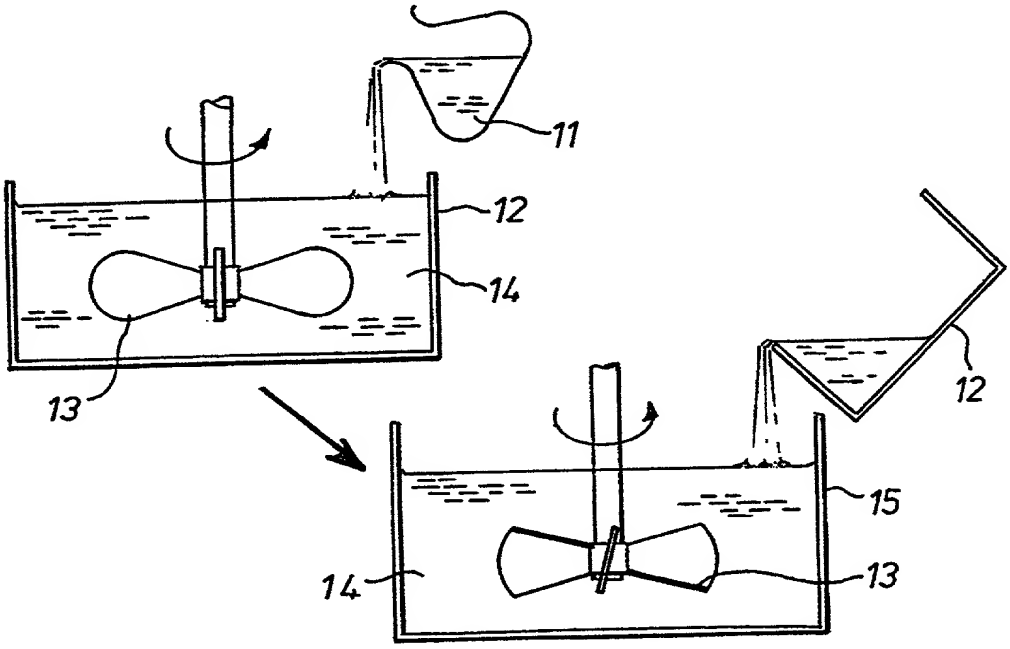


FIG.1

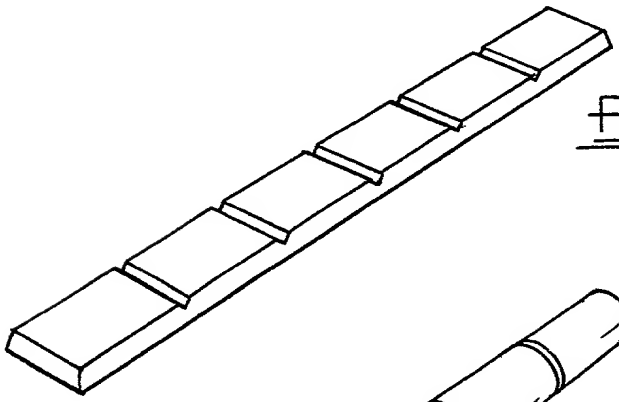


FIG. 2

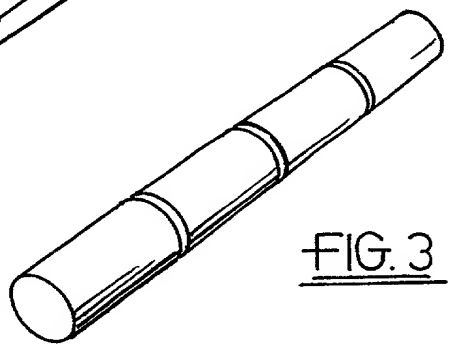


FIG. 3

DECLARATION AND POWER OF ATTORNEY U.S.A.

ALL PATENTS, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT; PARIS CONVENTION;
NON PRIORITY; OR PROVISIONAL APPLICATIONS

FOR ATTORNEYS' USE ONLY
ATTORNEYS' DOCKET NO.
P67280US0

As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled:

101 102

NICOTINE DELIVERY SYSTEMS

which is described and claimed in:

[ ] the attached specification

[X] PCT International Application No. **PCT/GB00/01807** filed **May 11, 2000**

[X] the specification in application Serial No. _____ filed **November 13, 2001**

(if applicable) and amended on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

103

Prior Foreign Application(s) (Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed
9911037.1	**GREAT BRITAIN**	**13 May 1999**	[X] Yes [ ] No
			[ ] Yes [ ] No
			[ ] Yes [ ] No

104

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.)	(Filing Date)	(Status: patented, pending, abandoned)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys (Registration No.) to prosecute this application, receive and act on instructions from my agent, and transact all business in the Patent and Trademark Office connected therewith HARVEY B. JACOBSON, JR (20,851), JOHN CLARKE HOLMAN (22,769), MARVIN R STERN (20,640); ALLEN S. MELSER (27,215); MICHAEL R. SLOBASKY (26,421); JONATHAN L. SCHERER (29,851); IRWIN M. AISENBERG (19,007); WILLIAM E PLAYER (31,409), YOON S. HAM (45,307) and NATHANIEL A. HUMPHRIES (22,772)

SEND CORRESPONDENCE TO: CUSTOMER NO. 00136 or	DIRECT TELEPHONE CALLS TO. (please use Attorney's Docket No) (202) 638-6666
JACOBSON HOLMAN **PROFESSIONAL LIMITED LIABILITY COMPANY** **400 SEVENTH STREET, N.W.** **WASHINGTON, D.C. 20004**	**JACOBSON HOLMAN** **PROFESSIONAL LIMITED LIABILITY COMPANY**

Inventor(s) name must include at least one unabbreviated first or middle name.

201 FULL NAME * OF INVENTOR	FAMILY NAME **MCNEIGHT**	GIVEN NAME **David**	MIDDLE NAME **Leslie**		
RESIDENCE & CITIZENSHIP	CITY **Cheshire** GBN	STATE OR FOREIGN COUNTRY **GREAT BRITAIN**	COUNTRY OF CITIZENSHIP **GREAT BRITAIN**		
POST OFFICE ADDRESS	POST OFFICE ADDRESS **Brow Top, Lees Lane, Wilmslow**	CITY **Cheshire**	STATE OR COUNTRY **GREAT BRITAIN**	ZIP CODE **SK9 2LR**	
202 FULL NAME * OF INVENTOR	FAMILY NAME	GIVEN NAME	MIDDLE NAME		
RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP		
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE	
203 FULL NAME * OF INVENTOR	FAMILY NAME	GIVEN NAME	MIDDLE NAME		
RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP		
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE	

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201*	SIGNATURE OF INVENTOR 202*	SIGNATURE OF INVENTOR 203*
X		
DATE 20 November 2001	DATE	DATE

[ ] Additional inventors are named on separately numbered sheets attached hereto.